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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,245	04/04/2001	Thyge Borup Hjorth	6184.200-US	2682

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EXAMINER
SHEIKH, HUMERA N

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 06/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/826,245	HJORTH ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2003 (paper no.9)* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Application

Receipt of the request for extension of time (1 month) and the Amendment, both filed 04/21/03 is acknowledged.

The 35 U.S.C. 112 second paragraph rejections have been *withdrawn.*

Claims 26-48 are pending. Claims 26-48 remain rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 26-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lohray et al. (WO 99/19313, collectively, "Lohray").

Lohray teaches a process for the preparation of (-) 3-[4-[2-phenoxazin-10yl)ethoxy]phenyl]-2-ethoxypropanoic acid compounds, their pharmaceutically acceptable salts and pharmaceutical compounds containing them (see reference page 1, lines 1-22). The compound (-) 3-[4-[2-phenoxazin-10yl)ethoxy]phenyl]-2-ethoxypropanoic acid has been found useful for the treatment and/or prophylaxis of insulin resistance (type 2 diabetes), hypertension, hyperlipidemia, obesity, etc. (pg. 1, lines 24 through pg. 2, line25). The pharmaceutical composition may be in the form of tablets, capsules, powders, syrups, suspensions, solutions and the like and may contain flavorants, sweeteners, excipients and the like in suitable solid or liquid carriers or diluents, or in suitable sterile media to form injectable solutions or suspensions. Such compositions contain from 1 to 20% of the active compound and the remainder of the composition being pharmaceutically acceptable carriers, diluents or solvents (pg. 31, lines 14-20); (pg. 32, lines 2-16). Example 7 demonstrates a process for the preparation of ethyl 3-[4-[2-(phenoxazin-10yl)ethoxy]phenyl-2-ethoxypropanoate wherein three methods (A-C) are recited. Method A recites that to a solution ethyl (E/Z)-3-[4-[2-(phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropenoate obtained in example 3 in dioxane was added and stirred at 25^0 C under 60 psi hydrogen pressure for 24 h. At the end of this time, the reaction mixture was filtered and the solvent was evaporated under reduced pressure. Similarly, Examples B and C form a white solid product

wherein Method C was a reaction mixture wherein water was added and extracted and organic extracts were washed with water, dried, filtered and evaporated.

The prior art teaches the same composition, method of use and a process for the preparation of a composition comprising the same compound (-) 3-[4-[2-phenoxazin-10yl)ethoxy]phenyl]-2-ethoxypropanoic acid as instantly claimed by the applicant (see claims 1 and 9). The prior art teaches such a composition comprising the same phenoxazine compound wherein a pharmaceutically acceptable carrier, diluent, excipient or solvate is included (claim 18). The composition can be in the form of a tablet, capsule, powder, syrup, solution or suspension (claim 19).

The instant claims differ from the reference of Lohray in that the instant claims have a limited scope. In actuality, the instant invention is a selection taken from the group of compounds taught by the prior art (Example 7 teaches the exact compound). The applicant is also attempting to differentiate from the prior art by claiming a compression technique in the process for preparation of the composition. However, compression techniques are well known to one of ordinary skill familiar with the pharmaceutical art for the formulation of tablets, capsules and the like.

Regarding the specified water content of the excipients, the water vapor pressure and the oxygen pressures, there is no criticality seen in the instantly claimed amounts or percentages, since the final end product of Lohray is a (-) 3-[4-[2-phenoxazin-10yl)ethoxy]phenyl]-2-ethoxypropanoic acid compound in the form of a tablet, powder or capsule, etc as desired by the applicant. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the

prior art unless there is evidence indicating such concentration or temperature is critical. Furthermore, in the absence of showing any unexpected results that accrue from the applicants claimed compound with excipients of a water content of below about 1%, one of ordinary skill in the art, could through routine or manipulative experimentation, obtain the best possible results.

Regarding the use of specified excipients as listed in applicant's claims 31-33 and 43-48, the examiner notes that these excipients are in fact, conventionally known excipients, readily used in pharmaceutical applications for the formulation of tablets, capsules and the like. As such, there is no showing of any unexpected results that accrues from the use of the specified excipients, as they are well known to one of ordinary skill in the art.

In conclusion, since Lohray et al. teach the same compound (-) 3-[4-[2-phenoxazin-10yl)ethoxy]phenyl]-2-ethoxypropanoic acid, composition and a similar process for the preparation of a composition comprising (-) 3-[4-[2-phenoxazin-10yl)ethoxy]phenyl]-2-ethoxypropanoic acid and the various forms of the compound (i.e., tablet, capsule, powder, etc.) (claims 18-19) as instantly claimed, one of ordinary skill in the art would have ample motivation to prepare such a composition comprising the same components for a similar intended purpose. The expected result would be a (-) 3-[4-[2-phenoxazin-10yl)ethoxy]phenyl]-2-ethoxypropanoic acid composition in solid form for the effective treatment and/or prophylaxis of insulin resistance (type 2 diabetes), hypertension, hyperlipidemia, obesity and various other cardiovascular, renal and related disorders.

Response to Arguments

Applicant's arguments filed 04/21/03 have been fully considered but they are not persuasive.

The applicant argued regarding the 35 U.S.C. 103(a) rejections stating, "There was no disclosure or suggestion in Lohray regarding compression procedures and no suggestions that it would be advantageous to obtain a composition having a low water content, nor is direction given as to what would be optimal."

The applicants arguments have been fully considered, but were not found to be persuasive. Lohray teaches a process for the preparation of (-) 3-[4-[2-phenoxazin-10yl)ethoxy]phenyl]-2-ethoxypropanoic acid compounds, their pharmaceutically acceptable salts and pharmaceutical compounds containing them (see reference page 1, lines 1-22). The composition can be in the form of a tablet, capsule, powder, syrup, solution or suspension (claim 19). The applicant's argument that Lohray does not teach a compression method is disagreed upon since Example 7 (A-C) clearly demonstrates a process for the preparation of the instant compound whereby a reaction mixture was obtained and formulated into a solid end product.

Further, the applicants argument that no suggestion was given regarding the advantages of a low water content is not persuasive since Lohray at page 31, line 15 clearly teaches the composition to be in suitable forms, such as tablets, capsules and powders. As such, these compressed solid forms would not contain significant amounts

of water, if any. In addition, it would have been obvious to one of ordinary skill in the pharmaceutical art to determine suitable amounts of water or any other component for that matter, through routine or manipulative experimentation based on the purpose intended. Lohray explicitly teaches solid dosage forms (i.e., tablet, powder, etc.) whereby high amounts of water would be exempt.

The prior art teaches a similar process for preparing a composition, which comprises the same compound ((-) 3-[4-[2-phenoxazin-10yl)ethoxy]phenyl]-2-ethoxypropanoic acid) as instantly claimed. Therefore the instant invention remains obvious and unpatentable over the prior art.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (703) 308-4429. The examiner can normally be reached on Monday through Friday from 7:00A.M. to 4:30P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

hns

June 20, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600